Observational Study

Higher Pain Catastrophizing and Preoperative Pain is Associated with Increased Risk for Prolonged Postoperative Opioid Use

Kevin R. Riggs, MD[1,2,6], Andrea L. Cherrington, MD[2], Stefan G. Kertesz, MD[1,2], Joshua S. Richman, MD, PhD[1,3], Aerin J. DeRussy, MPH[1], Allyson L. Varley, PhD[1], William C. Becker, MD[4,5], Melanie S. Morris, MD[1,3], Jasvinder A. Singh, MD[1,2], Alayne D. Markland, DO[1,2,6], and Burel R. Goodin, PhD[7]

From: [1]Birmingham VA Medical Center, Birmingham, AL; [2]Department of Medicine, University of Alabama at Birmingham, Birmingham, AL; [3]Department of Surgery, University of Alabama at Birmingham, Birmingham, AL; [4]VA Connecticut Healthcare System, West Haven, CT; [5]Department of Internal Medicine, Yale School of Medicine, New Haven, CT; [6]Geriatric Research, Education, and Clinical Center, Birmingham VA Medical Center, Birmingham, AL; [7]Department of Psychology, University of Alabama at Birmingham, Birmingham, AL

Address Correspondence:
Kevin R. Riggs, MD
Birmingham VA Medical Center, University of Alabama at Birmingham
1720 2nd Avenue South, MT 610
Birmingham, AL 35294-4410
E-mail: kriggs@uab.edu

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Background: Prolonged postoperative opioid use (PPOU) is considered an unfavorable post-surgical outcome. Demographic, clinical, and psychosocial factors have been associated with PPOU, but methods to prospectively identify patients at increased risk are lacking.

Objectives: Our objective was to determine whether an individual or a combination of several psychological factors could identify a subset of patients at increased risk for PPOU.

Study Design: Observational cohort study with prospective baseline data collection and passive outcomes data collection.

Setting: A single VA medical center in the United States.

Methods: Patients were recruited from a preoperative anesthesia clinic where they were undergoing evaluation prior to elective surgery, and they completed a survey before surgery. The primary outcome was PPOU, defined as outpatient receipt of a prescribed opioid 31 to 90 days after surgery as determined from pharmacy records. Primary covariates of interest were pain catastrophizing, self-efficacy, and optimism. Additional covariates included social and demographic factors, pain severity, medication use, depression, anxiety, and surgical fear.

Results: Of 123 patients included in the final analyses, 30 (24.4%) had PPOU. In bivariate analyses, preoperative opioid use and preoperative nonsteroidal anti-inflammatory drug use were significantly associated with PPOU. The combination of high pain catastrophizing and high preoperative pain (OR 3.32, 95% CI 1.41 - 7.79) was associated with higher odds of PPOU than either alone, and the association remained significant after adjusting for preoperative opioid use (OR 2.56, 95% CI 1.04 - 6.29).

Limitations: Patients were recruited from a single site, and the sample was not large enough to include potentially important variables such as procedure type.

Conclusions: A combination of high pain catastrophizing and high preoperative pain has the potential to be a clinically useful means of identifying patients at elevated risk of PPOU.

Key words: Postoperative pain, postoperative opioids, opioid prescribing, preoperative evaluation, pain catastrophizing

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The overuse of prescription opioids in the US over the past 2 decades has contributed to a crisis involving addiction, overdose, and suboptimal pain care (1,2). For years, a liberal supply of opioids for postoperative pain meant that surgery was frequently the initial exposure for many patients to the opioids that would cause future problems, such as dependence, misuse, or unintentional overdose (3). Recently,

efforts to ensure more judicious postoperative opioid prescribing have gained traction, including guidelines on appropriate prescription amounts (4) and implementing lower defaults in computerized order entry systems (5). Prolonged postoperative opioid use (PPOU) is now increasingly considered a negative outcome (3,6-8).

While definitions of PPOU vary (9-11), previous studies suggest that the majority of the initial supply of opioids provided after surgery go unused (12-14). Thus, the need for any refills after the initial supply may be the first warning that pain is being poorly controlled or that a problem related to opioids could be developing. However, being able to identify patients at greatest risk for PPOU before surgery could help target preemptive mitigation strategies to address not just the opioid receipt itself but the sustained pain concerns that often lead to PPOU.

An extensive body of literature documents the association of psychological and cognitive factors with chronic postoperative pain. Depression (15), anxiety (16), low self-efficacy (17), surgery-related fear (18), pain catastrophizing (16), low optimism (18), and numerous other factors have been shown in studies to be risk factors for chronic postoperative pain. Fewer studies have examined the association of psychological factors with PPOU per se, although pain catastrophizing (19,20) and mental health diagnoses (21-24) have been associated with PPOU. However, at present, the available data on predictors of PPOU is preliminary in nature, and as a result there are no clinically useful risk assessment tools, or guidance on how to utilize identified risk factors. Confirming the factors predisposing patients to PPOU could contribute to the development of clinical decision tools and aid in developing risk mitigation strategies that enhance the pain care provided to patients at greatest risk.

In this study, we sought to determine whether an individual or a combination of several psychological factors could identify a subset of patients at an increased risk for PPOU. The preliminary hypothesis was that a combination of psychosocial factors would serve as a stronger predictor of increased risk of PPOU. Specifically, the a priori hypothesis was that the combination of high pain catastrophizing, low self-efficacy, and low optimism would act as a marker of psychological vulnerability that would be associated with an increased risk of PPOU.

Methods

This was a prospective cohort study of 149 patients with planned elective outpatient surgery. This study and all procedures were reviewed and approved by the Institutional Review Board at the Birmingham VA Medical Center (VAMC) (approval # 01683) and carried out in a manner consistent with ethical research guidelines as outlined in the Declaration of Helsinki. All patients provided written informed consent prior to enrollment in the study.

Setting and Patients

We recruited a convenience sample of patients from a preoperative anesthesia evaluation clinic at the Birmingham VAMC from March 2019 to February 2020. All patients who undergo surgery at the Birmingham VAMC are required to be evaluated by nurses from the Department of Anesthesia in a preoperative clinic prior to their surgery. Research assistants were present on select days at an information table in the hallway outside of the preoperative clinic and recruited patients as they were entering or exiting the clinic. Given the nature of recruitment, we did not attempt to record the number of patients who were approached, and thus were not able to measure a recruitment rate. Our primary inclusion criterion was affirmation from the patient that they were planning upcoming surgery. We did not require that patients be scheduled for their surgery or be within a specific timeframe of the planned surgical date, as patients were often evaluated before the surgery was scheduled. Recruitment was not targeted based on any patient characteristics, but we attempted not to include patients who reported that they were planning to undergo eye surgery since patients undergoing these procedures are unlikely to be treated with opioids intraoperatively or postoperatively (25). Notably, this study included patients who were opioid-naïve and those who were currently receiving opioids. While the VA has implemented broad efforts to limit opioid prescribing, there were not any specific interventions related to this study to influence opioid prescribing or postoperative pain care (26).

Procedure

Once patients were enrolled, a trained research assistant administered an intake questionnaire on the same day, which included questions on demographics, preoperative medications, substance use, pain, and a battery of psychosocial measures (detailed below). In addition to survey data, we collected data from the electronic medical record, as detailed below. Patients were provided a $10 gift card as a participation incentive.

Survey Measures

Upon enrollment, patients completed a questionnaire with the assistance of a trained research assistant.

Demographics

Patients were asked about gender (male, female, other), race (6 categories, including other), ethnicity (Hispanic or non-Hispanic), education (initially 5 categories, later collapsed to 2), marital status (initially 6 categories, later collapsed to 2), and income (4 categories and an option "prefer not to answer"). Age was calculated from date of birth, and then categorized into 3 groups.

Preoperative Medication Use and Pain

Patients were asked about medication use in the 30 days before surgery, including opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and antidepressants. In each case, a non-inclusive list was provided with examples with response options "Yes," "No," or "I don't know." Pain was assessed using the PEG (27), a 3-item questionnaire that assesses pain intensity and interference with enjoyment of life and general activity on a scale of 0-10, and an average of the 3 scores was computed.

Pain Catastrophizing

Pain catastrophizing was assessed using the 13-item Pain Catastrophizing Scale (PCS) (28), which measures catastrophizing (a maladaptive tendency to assume the worst) across 3 dimensions: rumination, magnification, and helplessness. Questions are rated on a scale from 0 (not at all) to 4 (all the time), with a total possible score ranging from 0 to 52. However, after the study was underway, it became apparent that the PCS portion of the questionnaire excluded the response option "3 (to a great degree)." For the primary analysis, we computed the PCS using the usual scale. As a sensitivity analysis, we evaluated an alternative scoring of the PCS using a 0-3 scale (rescoring responses of 4 to 3). However, this scoring resulted in identical groupings of patients as above or below the median.

Self-Efficacy

Self-efficacy was assessed using the 4-item NIH Patient-Reported Outcomes Measurement Information System (PROMIS) General Self-Efficacy – Short Form (29), with 5 response options ranging from "I am not at all confident" to "I am very confident" and a total possible score of 4-20. An example item is "I can manage to solve difficult problems if I try hard enough."

Optimism

Optimism was assessed using the 10-item Life Orientation Test-Revised (LOTR) (30), with 5 response options ranging from strongly disagree to strongly agree, and a total possible score of 0-40. An example item is "I'm always optimistic about my future." In the LOTR, 4 items are reverse coded, with a response of agree responding to low optimism.

Depression and Anxiety

Depression was assessed using the 8-item Patient Health Questionnaire (PHQ-8) (31), with 4 response options ranging from "not at all" to "nearly every day," and a total possible score of 0-24. Anxiety was assessed using the 7-item General Anxiety Disorder (GAD-7) (32), with 4 response options ranging from "not at all" to "nearly every day" and a total possible score of 0-21.

Surgical Fear

Surgical fear was assessed using the 8-item Surgical Fear Questionnaire (SFQ) (33), with fear of different aspects of the upcoming surgery rated on a scale of 0-10, with a total possible score of 0-80. An example item is "I am afraid of the operation."

Approach to Missing Data

In several instances, 1 or 2 items from a multiple-item instrument were left blank, possibly due to participant or research assistant error. In these cases, we imputed the missing item based on the average of other responses. One participant discontinued the survey partway through. For this person, we included the instruments that had been completed and did not include instruments that were skipped.

In addition to the prospective data elements above, we extracted some pre-specified data elements from the electronic medical record. One author (anonymized for review) reviewed each local chart to ascertain whether an operation occurred in the 90 days after enrollment. For patients with an operation identified, the Anesthesia Society of America Physical Status (ASA-PS) and anesthesia type (general or other) were recorded from the day-of-surgery anesthesia attending note. Operation type was recorded from the operative note and grouped together using other published schemas as a guide (34). Postoperative disposition (home vs inpatient admission) was also ascertained by reviewing the local electronic medical record. Preoperative medical comorbidities and postoperative opioid use were extracted from the

centralized electronic medical record (corporate data warehouse). We queried diagnosis codes from the 12 months prior to study enrollment to calculate an Elixhauser score (35). We queried outpatient pharmacy fills of opioid agonists, and observed hydrocodone, oxycodone, morphine, tramadol, and buprenorphine (exclusively sublingual buprenorphine-naloxone). Because buprenorphine is often used to treat opioid use disorder rather than pain, we excluded patients who had any fills of buprenorphine in the 3 months prior to their operation.

The primary outcome was PPOU, defined as outpatient receipt of any opioid fill of any duration between 31 to 90 days after surgery. We used this definition to capture receipt of opioids beyond the typical 30-day postoperative window when most postoperative complications occur. The need for any refills after the initial supply may be the first warning that pain is being poorly controlled or that a problem related to opioids could be developing, and thus opioid use during this time period was designated as "prolonged"(36).

Statistical Analyses

First, we examined the characteristics of all patients. We compared baseline data for those included in the final analyses (n = 123) with those excluded because they did not undergo surgery (n = 16), underwent eye surgery (n = 4), or had fills of buprenorphine within 3 months prior to surgery (n = 6). We then compared the characteristics of those who had PPOU and those who did not. Categorical variables were compared using chi-squared, and continuous variables were compared using a t-test.

In order to determine whether combinations of psychosocial factors could be used to identify patients at increased risk of PPOU, we created composite variables identifying patients with high scores on multiple assessments. To create these composite variables, we identified the median value of each of the psychological and pain variables and then created an indicator variable for patients who had worse than median scores on the variables of interest. In addition to the main composite of interest, we also tested various combinations of variables with $P < 0.1$ on bivariate analyses (37). We ran logistic regression models with the variables of interest and their combination with PPOU as the dependent variable. We repeated logistic regression models and included preoperative opioid use as a covariate (for combination variables that did not include preoperative opioid use).

Results

A total of 149 patients were enrolled, and 123 were included in the final analyses. Sixteen patients were excluded because they did not undergo any operation within 90 days of enrollment; 4 were excluded because they underwent eye surgery; and 6 were excluded because they had filled buprenorphine in the 3 months prior to their operation. Participant demographics and baseline data of the full cohort are shown in Appendix Table 1. Excluded patients were more likely to be taking preoperative opioids (50.0% vs 22.8%, $P = 0.005$) and more likely to have low optimism (84.6% vs 47.2%, $P = 0.001$).

Demographics and baseline data for patients included in the final analyses are shown in Table 1. The mean age of patients was 61.1 (SD 11.6), and 9.8% were female. A total of 30 patients (24.4%) had PPOU. In bivariate analyses, those with PPOU were more likely to be taking preoperative opioids (43.3% vs 16.1%, $P = 0.002$) and NSAIDs (63.3% vs 36.6%, $P = 0.01$). High pain catastrophizing (63.3% vs 44.1%, $P = 0.067$) and high preoperative pain ($P = 0.093$) were not statistically associated with PPOU, but given $P < 0.1$, these variables were explored further in models with combination variables.

The results of logistic regression models examining the association of characteristics of interest and combinations of characteristics with PPOU are shown in Table 2. Pain catastrophizing, self-efficacy, and optimism were not significantly associated with PPOU, and neither were any combinations of those factors, either before or after adjusting for preoperative opioid use. However, each of the combinations of high pain catastrophizing, high preoperative pain, preoperative NSAIDs, and preoperative opioids were significantly associated with PPOU. The combination of high pain catastrophizing and high preoperative pain (OR 3.32, 95% CI 1.41 - 7.79) was associated with higher odds of PPOU than either alone and was the only combination assessed that remained significantly associated with PPOU after adjusting for preoperative opioid use (OR 2.56, 95% CI 1.04 - 6.29).

Discussion

In this study of patients undergoing a variety of operations, 24.4% had continued opioid use between 31 and 90 days after surgery. While preoperative opioid use was a strong predictor of postoperative opioid use, the combination of high preoperative pain and high pain catastrophizing was associated with PPOU, even

after adjusting for preoperative opioid use. We think this could be a promising way to screen for elevated risk for PPOU in both opioid naïve patients and those already on opioids preoperatively.

The ability to efficiently identify patients at elevated risk for PPOU has important clinical implications, most notably facilitating the development and delivery of interventions to mitigate risk. Previous studies have suggested that approximately 2% to 6% of opioid naïve patients develop PPOU (11). This low outcome rate makes it unlikely that even moderate-intensity interventions would be cost-effective in general populations. Furthermore, the ability to identify patients at increased risk would allow for more testing of potential interventions by allowing for smaller sample sizes. For example, Dindo et al (38) recently evaluated the feasibility of a 1-day preoperative workshop based on Acceptance and Commitment Therapy (38). In that study, eligibility for the study was based on either preoperative pain or a combination of preoperative pain and either depression or anxiety. While the ability of that criteria to identify patients at elevated risk of prolonged opioid use has not been formally evaluated to our knowledge, our identified features of preoperative pain and pain catastrophizing could serve as potential criteria for future studies.

The precise point at which continued opioid use after surgery becomes problematic is uncertain (9). Opioids are the

Table 1. *Baseline characteristics of included patients, with and without (PPOU).*

	Total, n (%) n = 123	**PPOU, n (%) n = 30**	**No PPOU, n (%) n = 93**	***P* value**
Age, mean (SD)	61.1 (11.6)	61.7 (8.4)	60.9 (12.5)	0.752
Age Category				0.170
18-44	15 (12.2%)	2 (6.7%)	13 (14.0%)	
45-64	60 (48.8%)	19 (63.3%)	41 (44.1%)	
65+	48 (39.0%)	9 (30.0%)	39 (41.9%)	
Female	12 (9.8%)	2 (6.7%)	10 (10.8%)	0.512
Race				0.484
White	56 (46.5%)	12 (40.0%)	44 (47.3%)	
Black	67 (53.5%)	18 (60.0%)	49 (52.7%)	
Marital Status (n = 122)				0.403
Married	65 (53.3%)	14 (46.7%)	51 (55.4%)	
Not married	57 (46.3%)	16 (53.3%)	41 (44.6%)	
Education				0.505
High school or less	43 (35.0%)	12 (40.0%)	31 (33.3%)	
Some college or more	80 (65.0%)	18 (60.0%)	62 (66.7%)	
Annual Income				0.404
Less than $30,000	53 (43.1%)	14 (46.7%)	39 (41.9%)	
$30,000 to $55,000	39 (31.7%)	12 (40.0%)	27 (29.0%)	
$55,000 to $95,000	24 (19.5%)	4 (13.3%)	20 (21.5%)	
More than $95,000	4 (3.3%)	0	4 (4.3%)	
No answer	3 (2.4%)	0	3 (3.2%)	
Elixhauser Count, mean (SD)	4.2 (2.7)	4.2 (2.8)	4.3 (2.7)	0.978
Elixhauser Count				0.440
0-2	39 (31.7%)	8 (26.7%)	31 (33.3%)	
3-4	34 (27.6%)	11 (36.7%)	23 (24.7%)	
5+	50 (40.7%)	11 (36.7%)	39 (41.9%)	
Preoperative Medications				
Opioids	28 (22.8%)	13 (43.3%)	15 (16.1%)	0.002
NSAIDs	53 (43.1%)	19 (63.3%)	34 (36.6%)	0.010
Antidepressants	39 (31.7%)	12 (40.0%)	27 (29.0%)	0.262
PEG, mean (SD) (n = 122)	4.9 (3.4)	6.0 (3.3)	4.5 (3.4)	0.043
High preoperative pain (PEG > 5) n = 122	57 (46.7%)	18 (60.0%)	39 (42.4%)	0.093
Psychological Test Outcomes				
PCS, mean (SD)	14.2 (14.0)	17.7 (15.2)	13.0 (13.5)	0.114
High pain catastrophizing (PCS > 11)	60 (48.8%)	19 (63.3%)	41 (44.1%)	0.067
GSE-SF, mean (SD)	12.7 (3.8)	12.9 (3.8)	12.6 (3.8)	0.662
Low self-efficacy (GSE-SF < 14)	57 (46.3%)	12 (40.0%)	45 (48.4%)	0.642
LOTR, mean (SD)	26.9 (6.1)	26.4 (6.2)	27.0 (6.1)	0.604
Low optimism (LOTR < 27)	58 (47.2%)	17 (56.7%)	41 (44.1%)	0.230
SFQ, mean (SD)	16.6 (18.9)	19.0 (21.4)	15.9 (18.1)	0.428
High surgical fear (SFQ > 8)	59 (48.0%)	15 (50.0%)	44 (47.3%)	0.798

Table 1 (continued). *Baseline characteristics of included patients, with and without (PPOU).*

	Total, n (%) n = 123	PPOU, n (%) n = 30	No PPOU, n (%) n = 93	*P* value
PHQ-8, mean (SD) n = 122	6.5 (6.0)	7.6 (6.6)	6.1 (5.8)	0.245
High depression (PHQ-8 score >5) n = 122	54 (44.3%)	15 (50.0%)	39 (42.4%)	0.466
GAD-7, mean (SD) n = 122	5.7 (6.6)	7.0 (7.3)	5.3 (6.4)	0.231
High anxiety (GAD-7 score > 3) n = 122	55 (45.1%)	14 (46.7%)	41 (44.6%)	0.841
Surgical Factors				
Surgery Type				0.415
Abdominal	11 (8.9%)	4 (13.3%)	7 (7.5%)	
ENT	9 (7.3%)	5 (16.7%)	4 (4.3%)	
Fistula	10 (8.1%)	2 (6.7%)	8 (8.6%)	
Hand	12 (9.8%)	1 (3.3%)	11 (11.8%)	
Hernia	7 (5.7%)	1 (3.3%)	6 (6.5%)	
Joint	7 (5.7%)	1 (3.3%)	6 (6.5%)	
Other Orthopedic	11 (8.9%)	2 (6.7%)	9 (9.7%)	
Skin	6 (4.9%)	1 (3.3%)	5 (5.4%)	
Spine	7 (5.7%)	3 (10.0%)	4 (4.3%)	
Urology	21 (17.1%)	4 (13.3%)	17 (18.3%)	
Other	22 (17.9%)	6 (20.0%)	16 (17.2%)	
Postoperative Inpatient Admission	45 (36.6%)	14 (46.7%)	31 (33.3%)	0.187
General Anesthesia	105 (85.4%)	24 (80.0%)	81 (87.1%)	0.339
ASA-PS score, mean (SD)	2.80 (0.6)	2.87 (0.6)	2.77 (0.6)	0.455
ASA-PS score				0.711
I	1 (0.8%)	0	1 (1.1%)	
II	33 (26.8%)	7 (23.3%)	26 (28.0%)	
III	79 (64.2%)	20 (66.7%)	59 (63.4%)	
IV	10 (8.1%)	3 (10.0%)	7 (7.5%)	

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; GAD, General Anxiety Disorder; GSE-SF, General Self-Efficacy – Short Form; NSAID, non-steroidal anti-inflammatory drug; SFQ, Surgical Fear Questionnaire; PCS, Pain Catastrophizing Scale; PHQ, Patient Health Questionnaire; PPOU, prolonged postoperative opioid use; LOTR, Life Orientation Test-Revised

primary means of controlling perioperative pain, and most patients are treated with some opioids at the time of surgery (39,40). Postoperative opioid use tends to decrease over time during the first year after surgery (i.e., fewer patients continue to take opioids at 6 months after surgery than at 3 months, and fewer still at 12 months) (41). While the terminology describing prolonged postoperative opioid use is inconsistent (sometimes termed "prolonged," "persistent," or "chronic"), and definitions have ranged from continued use 30 days after surgery (42) to use a year or more after surgery (10,11), evidence suggests that risk of misuse increases with duration (43). Therefore, continued opioid use earlier in the postoperative course may be a more sensitive marker for future problems than continued use at later points. In our study, we chose a fill during the 31-90 day window because it was likely to represent an additional refill after the initial postoperative prescription. While not all patients with opioid fills 31-90 days postoperatively will go on to develop persistent use, we believe that a more sensitive measure is appropriate when considering how to identify a population that may warrant risk mitigation.

The strong association of preoperative opioid use with PPOU in our study (even though we did not attempt to determine whether preoperative use was "chronic") is not surprising, as preoperative opioid use has consistently been found to be the strongest predictor of postoperative opioid use (44-48). Much of the literature on PPOU has focused on opioid-naïve patients (6,23), but previous studies suggest that a substantial proportion of patients who use opioids chronically before surgery cease their opioid use at some point the year after surgery (49,50). Therefore, when considering potential risk mitigation efforts, we believe it would be a mistake to focus exclusively on avoiding PPOU in opioid-naïve patients and ignore the possibility that the postoperative period may be a unique opportunity for patients who had previously been on chronic opioids to reconsider their continued use. Our study's inclusion of previous opioid users and opioid-naïve patients and our findings that preoperative pain and high pain catastrophizing were associated with increased risk of PPOU even after adjusting for preoperative opioid use makes

Table 2. *Association of characteristics and combinations with postoperative opioid fills 31-90 days after surgery, N = 123.*
*N is less than 123 due to missing data for one patient in the pain measure

	n with opioid fill / n with characteristic (%)	Model 1: Characteristic only OR (95% CI)	Model 2: Characteristic adjusted for preoperative opioids OR (95% CI)
Characteristic			
Primary Characteristics and Combinations			
High pain catastrophizing	19 / 60 (31.7%)	2.19 (0.94 - 5.11)	1.69 (0.69 - 4.14)
Low self-efficacy	12 / 57 (21.1%)	0.71 (0.31 - 1.64)	0.72 (0.31 - 1.74)
Low optimism	17 / 58 (29.3%)	1.66 (0.72 - 3.80)	1.49 (0.63 - 3.53)
High pain catastrophizing and low self-efficacy	10 / 33 (30.3%)	1.52 (0.62 - 3.72)	1.34 (0.52 - 3.41)
High pain catastrophizing and low optimism	12 / 34 (35.3%)	2.15 (0.90 - 5.15)	1.66 (0.66 - 4.20)
Low self-efficacy and low optimism	9 / 38 (23.7%)	0.95 (0.39 - 2.32)	0.92 (0.36 - 2.34)
High pain catastrophizing and low self-efficacy and low optimism	8 / 24 (33.3%)	1.75 (0.66 - 4.63)	1.38 (0.49 - 3.87)
Secondary Characteristics and Combinations			
High Pain (n = 122)*	18 / 57 (31.6%)	2.04 (0.88 - 4.72)	1.45 (0.59 - 3.60)
Preoperative NSAIDS	19 / 53 (35.8%)	3.00 (1.28 - 7.04)	2.95 (1.21 - 7.16)
Preoperative opioids	13 / 28 (46.4%)	3.98 (1.60 - 9.87)	NA
High pain catastrophizing and high pain (n = 122)*	17 / 43 (39.5%)	3.32 (1.41 - 7.79)	2.56 (1.04 - 6.29)
High pain catastrophizing and preoperative NSAIDS	12 / 30 (40.0%)	2.78 (1.14 - 6.79)	2.45 (0.96 - 6.21)
High pain and preoperative NSAIDS	11 / 27 (40.7%)	2.79 (1.11 - 6.97)	2.05 (0.77 - 5.45)
High pain catastrophizing and preoperative opioids	11 / 20 (55.0%)	5.40 (1.96 - 14.86)	NA
High pain and preoperative opioids	11 / 21 (52.4%)	4.81 (1.78 - 12.94)	NA
Preoperative opioids and preoperative NSAIDS	7 / 14 (50.0%)	3.74 (1.19 - 11.74)	NA

*n is less than 123 due to missing data for one patient in the pain measure

these findings potentially more useful when considering risk in populations regardless of prior opioid use.

While pain catastrophizing has been shown in previous studies to be associated with postoperative pain and opioid use, there are several barriers to more widespread clinical use. The first challenge is the lack of well-defined cut points to signify high pain catastrophizing using the PCS. In our study, we simply dichotomized based on the median value in our population, and we considered any value greater than 11 to be high, but different cut points have been used in other studies. Sullivan et al (28) proposed a cut point of greater than 30 when the PCS was initially described, which corresponded to the 75th percentile of the distribution of PCS scores in their population of patients with chronic pain, and other studies have utilized this cut point (51). Other studies have used other cut points, such as 16 (52). More studies that evaluate the clinical utility of various thresholds are needed. An additional challenge to the more widespread clinical use of pain catastrophizing is the potentially stigmatizing nature of the term, and efforts to consider potential alternatives are ongoing (53).

Our finding that NSAID use was among the factors most associated with PPOU is also not surprising. While NSAID use has not consistently been evaluated in prior studies of PPOU (48) (potentially because of the availability of NSAIDs without a prescription makes it more difficult to study using claims data or medical record data), it has been shown to be associated with PPOU in other studies (41). Furthermore, chronic pain conditions (11), including arthritis (6), have consistently been shown to be associated with PPOU. It is likely that preoperative NSAID use is a marker of either worse preoperative pain or of a condition such as osteoarthritis that is associated with worse postoperative pain.

Our study is subject to several important limitations. First, our study had a relatively small sample size. This small sample size did not allow us to account for surgery type in our models. Previous studies have shown that the risk for prolonged postoperative opioid use varies among different surgery types (7), so future

studies could assess whether a combination of preoperative pain and pain catastrophizing works more or less well across different surgery types. The small sample size also increases the risk of a type I error, and future studies should confirm whether preoperative pain and pain catastrophizing can effectively stratify risk before widespread clinical adoption. Second, our primary outcome was based on prescription fill data, and it is not possible to know whether the medications were actually consumed and whether they were being prescribed for pain directly related to the recent surgery or some other unrelated medical condition. Third, our prescription fill data was only from the VA system, so it is possible that we may have failed to capture opioid medications filled outside of the VA system. Finally, our exclusion of a PCS response option on our survey introduced potential measurement error into our data. However, sensitivity analyses yielded identical results, which is reassuring.

Conclusion

In conclusion, this study of mixed surgical patients, including opioid-naïve and prior opioid users, found that the combination of high preoperative pain and high pain catastrophizing were associated with PPOU, even after adjusting for preoperative opioid use. These relatively simple measures could be the basis for a clinically useful way to screen for elevated risk for PPOU. The ability to identify patients before surgery who are at increased risk would facilitate the development and delivery of interventions to improve pain and opioid-related outcomes in patients undergoing surgery.

Disclosures

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Appendix Table 1. *Baseline characteristics of included and non-included patients.*

	All n = 149, n (%)	**Included n = 123, n (%)**	**Non-included n = 26, n (%)**	***P* value**
Age, mean (SD)	61.6 (11.4)	61.1 (11.6)	64.0 (10.1)	0.237
Age Category				0.434
18-44	16 (10.7%)	15 (12.2%)	1 (3.8%)	
45-64	73 (49.0%)	60 (48.8%)	13 (50.0%)	
65+	60 (40.3%)	48 (39.0%)	12 (46.2%)	
Female	14 (9.4%)	12 (9.8%)	2 (7.7%)	0.743
Race				0.509
White	70 (47.0%)	56 (46.5%)	14 (53.8%)	
Black	79 (53.0%	67 (53.5%)	12 (46.2%)	
Marital Status n = 148				0.509
Married	77 (52.0%)	65 (53.3%)	12 (46.2%)	
Not married	71 (48.0%)	57 (46.3%)	14 (53.8%)	
Education				0.479
High school or less	54 (36.2%)	43 (35.0%)	11 (42.3%)	
Some college or more	95 (63.8%)	80 (65.0%)	15 (57.7%)	
Annual Income				0.069
Less than $30,000	62 (41.6%)	53 (43.1%)	9 (34.6%)	
$30,000 to $55,000	45 (30.2%)	39 (31.7%)	6 (23.1%)	
$55,000 to $95,000	30 (20.1%)	24 (19.5%)	6 (23.1%)	
More than $95,000	5 (3.4%)	4 (3.3%)	1 (3.8%)	
No answer	7 (4.7%)	3 (2.4%)	4 (15.4%)	
Elixhauser Count, mean (SD)	4.2 (2.7)	4.2 (2.7)	4.4 (2.6)	0.725
Elixhauser Count				0.324
0-2	45 (30.2%)	39 (31.7%)	6 (23.1%)	
3-4	45 (30.2%)	34 (27.6%)	11 (42.3%)	
5+	59 (39.6%)	50 (40.7%)	9 (34.6%)	
Preoperative Medications				
Opioids	41 (27.5%)	28 (22.8%)	13 (50%)	0.005
NSAIDs	67 (45.0%)	53 (43.1%)	14 (53.8%)	0.316
Antidepressants	49 (32.9%)	39 (31.7%)	10 (38.5%)	0.505
PEG, mean (SD) n = 148	5.0 (3.3)	4.9 (3.4)	5.9 (2.9)	0.169
High preoperative pain (PEG > 5) n = 148	72 (48.3%)	57 (46.7%)	15 (57.7%)	0.310
Psychological test outcomes				
PCS, mean (SD)	14.3 (13.8)	14.2 (14.0)	14.9 (13.1)	0.806
PCS > 11	74 (49.7%)	60 (48.8%)	14 (53.8%)	0.639
GSE-SF, mean (SD)	12.4 (3.9)	12.7 (3.8)	11.2 (3.9)	0.085
Low self-efficacy (GSE-SF < 14)	74 (49.7%)	57 (46.3%)	17 (65.4%)	0.078
LOTR, mean (SD)	26.2 (6.3)	26.9 (6.1)	23.0 (6.3)	0.004
Low optimism (LOTR < 27)	80 (53.7%)	58 (47.2%)	22 (84.6%)	0.001
SFQ, mean (SD)	16.1 (18.8)	16.6 (18.9)	13.4 (18.3)	0.429
High surgical fear (SFQ > 8)	70 (47.0%)	59 (48.0%)	11 (42.3%)	0.599
PHQ-8, mean (SD) n = 148	6.9 (6.5)	6.5 (6.0)	8.7 (8.2)	0.104

Appendix Table 1 (continued). *Baseline characteristics of included and non-included patients*.

	All n = 149, n (%)	**Included n = 123, n (%)**	**Non-included n = 26, n (%)**	***P* value**
High depression (PHQ-8 score > 5) n=148	68 (45.6%)	54 (44.3%)	14 (53.8%)	0.373
GAD-7, mean (SD) n = 148	6.0 (6.9)	5.7 (6.6)	7.2 (8.0)	0.331
High anxiety (GAD-7 score > 3) n = 148	67 (45.3%)	55 (45.1%)	12 (46.2%)	0.921

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; GAD, General Anxiety Disorder; GSE-SF, General Self-Efficacy – Short Form; NSAID, non-steroidal anti-inflammatory drug; SFQ, Surgical Fear Questionnaire; PCS, Pain Catastrophizing Scale; PHQ, Patient Health Questionnaire; PPOU, prolonged postoperative opioid use; LOTR, Life Orientation Test-Revised